antidepressant class medications, anticonvulsant class medications, combinations of psychostimulant and antidepressant class medications, combinations of anticonvulsant and antidepressant class medications, combinations of psychostimulant, antidepressant, and anticonvulsant class medications.

The present invention also includes a method for computerized generation of clinical reports that integrates interpretive information from medical professionals with results of medication responsivity evaluation.

BRIEF DESCRIPTION OF THE FIGURES

The present invention may be understood more fully by reference to the following detailed description of the preferred embodiment of the present invention, illustrative examples of specific embodiments of the invention and the appended figures in which Fig. 1 illustrates a method of the present invention where: step 1 of Fig. 1 corresponds to elements 1 and 2 of the invention described below; step 2 corresponds to elements 3, 4, and 3; step 3 to elements 6 and 7; step 4 to element 8; and step 5 to elements 9 and 10.

DETAILED DESCRIPTION OF THE INVENTION

More specifically, the following steps are employed:

1) The EEG is recorded using electrodes placed on the patient's scalp, and the EEG data is stored in a digital format using a standardized protocol available on one of a number of commercially available instruments (current manufacturers include Cadwell Laboratories, Bio-Logic Systems Corp., Nicolet Biomedical, Oxford Instruments, among others). The International 10-20 System convention is used for determining the location of electrodes placed on the scalp. It is the responsibility of the recording facility to collect data in accordance with procedural specifications.

2) The following patient criteria apply:

a) Patient must have received a psychiatric diagnosis as specified in the Diagnostic and Statistical Manual, currently the Fourth Edition (DSM-IV).

b) Ages between six and ninety.

c) Patient is taking no medications. All medications potentially influence the EEG and must be discontinued or avoided for seven half-lives prior to baseline EBG examination. This includes "over the counter" sleeping pills, pain medication, nutritional health supplements and mega-vitamins.

d) Insulin, thyroid, estrogen, progesterone and other hormone replacement agents are not excluded. Some cardiac agents are included in the reference population of after the age of fifty-five.

e) Patients with any of the characteristics listed below are not suitable for prediction of medication responsivity based on EEG analysis:

(i) intramuscular depo-neuroleptic therapy within the preceding twelve months

(ii) a history of craniotomy with or without metal prostheses

(iii) a history of cerebrovascular accident

(iv) spikes or extreme low voltage on the conventional EEG

(v) a current diagnosis of seizure disorder

(vi) a diagnosis of dementia

(vii) mental retardation

(viii) current use of marijuana, cocaine, hallucinogens or other drugs of abuse

(ix) inability to remain medication-free and drug-free for seven half-lives of the current agent(s) prior to EEG recording

(x) significant abnormality of the CBC, chemistry or thyroid panel with TSH until corrected

f) A "positive" Urine Drug Screen (UDS) interferes with medication prediction methods. Studies are processed only if the UDS is negative just prior to recording the digital EEG.

3) The digital EEG data computer file is packaged along with additional patient identifying information using packaging and transmission software. The patient information includes:

a) name
b) date of birth
c) referring physician
d) handedness
e) height
f) weight
g) date of test
h) patient ID (social security number)

Packaging refers to compression of the computer file and encryption of the file so that it cannot be opened or examined by anyone other than at the processing center. The data transfer is rigorously secured to protect the confidentiality of patient records. The EEG files are encrypted at the recording facility with a key known only to processing center. The patient ID is transformed using a algorithm so that even in the case of mail routing error there is no way to associate the data with an individual. The data is compressed and protected with an additional password and data files are transmitted to a secure site. These steps mean that the patient data are protected against even purposeful attempts to intercept and read them.

The transmittal of the EEG file and related patient information is tracked as it is packaged, sent, processed, and returned. All log entries include dates and times calibrated to GMT.

The computer operating system preferred to run the packaging and report transmission software is currently Microsoft Windows 95/98. The following hardware and software is preferred:

Hardware Requirements

Operating System: Windows 95 or Windows 98
Processor: 486, 133 MHZ.
Monitor and Video Card capable of displaying 256 colors.
Disk Space: 35 MB
RAM: 16MB
CD-ROM Drive if installing from CD-ROM
Modem: 33.6 KBaud
Internet Connection with approved Internet Service Provider

Software Requirements

Adobe Acrobat Reader Version 3.01
Microsoft Internet Explorer 4.0 or above
The packaging and transmission software

4) The computer file is transferred off-hours using standard commercially available file transfer protocols (FTP) via the Internet, to a designated processing site. A special feature of the packaging and transmission software exists to allow immediate transfer of files for priority reporting if requested. The processing site monitors the transfer in order to detect

the arrival of new computer files. When a new file is received, it is forwarded for professional interpretation, if requested, and specialized report generation.

5) The file is decompressed and decrypted at the processing site. Experienced technical and professional personnel then review the EEG signals and sections of the recording identified as containing signals generated by extracerebral sources are deleted from subsequent analyses. The samples of EEG selected for inclusion in analysis are then passed to the first stage of analysis.

6) The first stage of analysis includes computations that extract a standard set of features from the EEG. Quantitative spectral analysis provides commonly used measures of EEG power and relative power. Power is the square of amplitude; amplitude units are in microvolts (μV), power units are microvolts squared(μV^2). Relative power is a measure of the proportion of power in a given frequency band compared to the total band power at a given electrode. Frequency bands are defined as delta, .5 - 2.5 Hz.; theta, 2.5 - 7.5 Hz.; alpha, 7.5 - 12.5 Hz., and beta, 12:5 - 32Hz. The total band is .5 to 32 Hz.

EEG coherence, a commonly used measure of the similarity of activity for a pair of two scalp electrodes, also is extracted by spectral analysis for all interhemispheric and intrahemispheric sets of electrode pairs, for each frequency band as defined above.

Commonly used measures of peak frequency within each defined frequency band are computed.

Combinations of power and coherence measures over defined sets of scalp electrodes are also computed.

7) Features extracted from individual EEG data by quantitative spectral and statistical analysis are further compared to two distinct databases. In the second stage of analysis, Z-scores representing deviations from a nonsymptomatic reference population are computed. This reference population, often referred to as the "Neurometric" database, contains 2082 quantitative EEG measures including absolute power, relative power, coherence, symmetry, and mean frequency of the delta, theta, alpha and beta frequency bands of the EEG at every electrode position of the International 10-20 System for individuals from 6 to 92 years (database #1). The z-score value obtained by comparison of individual's data to the age appropriate subset of the database represents the patient's statistical deviation from the reference database.

8) The third stage of processing involves medication response prediction using the patient database(database #2). This prediction is made by first identifying the pattern of EEG deviations from the reference database. Individual patient deviation is then compared with the characteristic features of the population of patients whose medications and treatment outcomes are known. A rule-based classifier is applied to estimate the likelihood that a patient EEG contains a pattern known to be responsive to a given agent, class of agents, or combination of agents or classes of agents. The EEG variables currently used by the classifier are shown in Tables 1-4, below.

Column Heading	Description of Abbreviation	Column Heading	Description of Abbreviation
Table 1		**Table 2**	
RMAD	Relative power monopolar anterior delta	FMAD	Frequency monopolar anterior delta
RMPD	posterior data	FMPD	posterior delta
RMAT	anterior theta	FMAT	anterior theta
RMPT	posterior theta	FMPT	posterior theta
RMAA	Anterior alpha	FMAA	anterior alpha
RMPA	Posterior alpha	FMPA	posterior alpha
RMAB	Anterior beta	FMAB	anterior beta
RMPB	posterior beta	FMPB	posterior beta
CEAD	Coherence interhemispheric anterior delta	AADL	Asymmetry intrahemispheric delta - left
CEPD	Posterior delta	AADR	delta - right
CEAT	anterior theta	AATL	theta - left
CEPT	posterior theta	AATR	theta - right
CEAA	anterior alpha	AAAL	alpha - left
CEPA	Posterior alpha	AAAR	alpha - right
CEAB	Anterior beta	AABL	beta - left
CEPB	posterior beta	AABR	beta - right

Table 3		Table 4	
AED	Asymmetry monopolar interhemispheric delta	CEBD	Coherence interhemispheric bipolar delta
AET	Theta	CEBT	Theta
AEA	Alpha	CEBA	Alpha
AEB	Beta	CEBB	Beta
AEBD	Asymmetry bipolar interhemispheric delta	RBDL	Relative power bipolar delta left
AEBT	Theta	RBDR	Delta - right
AEBA	Alpha	RBTL	Theta - left
AEBB	Beta	RBTR	Theta - right
CADL	Coherence intrahemispheric delta - left	RBAL	Alpha - left
CADR	Delta - right	RBAR	Alpha - right
CATL	Theta - left	RBBL	Beta - left
CATR	Theta - right	RBBR	Beta - right
CAAL	Alpha - left		
CAAR	Alpha - right		
CABL	Beta - left		
CABR	Beta - right		

9) A formal report for the referring clinician is generated. The report is returned in a format that cannot be modified by the client (Adobe Systems, Inc., "portable document format", or "PDF"). This report contains certain elements as specifically requested by the referring clinician. These elements may include a professional medical interpretation of the digital EEG tracing, a presentation of selected features extracted by quantitative EEG analysis, a presentation of deviations from the Neurometric database, and a statement of the likelihood of favorable pharmacotherapeutic outcome based on comparison with patients having similar EEG features in the patient database #2. The treating physician is responsible for any medication selection, titrating of dosage and monitoring the patient for side effects and is instructed to incorporate results of reports with the psychiatric assessment to develop into an overall clinical treatment plan.

10) The report is returned and may be downloaded by the client on a regular schedule, using the packaging and transmission software for viewing and printing the report by the client at the recording site. PDF files are opened and displayed using an interface to Adobe Acrobat Reader (TM) software. Reports may be printed on any operating system compatible printer.

11) Follow up EEG recordings can then be used to track changes produced by administration of medications by repeating the entire process outlined above. For follow up studies, the patient also is interviewed by the treating physician and Clinical Global Improvement (CGI) is scored. A score of -1 indicates an adverse effect, 0 no improvement, 1 minimal or mild improvement, 2 moderate improvement, and 3 marked improvement or remission of symptoms. The CGI scores are sent to the processing center and are reported along with changes, expressed as difference scores, on variables shown in Tables 1-4 above.

The invention described and claimed herein is not to be limited in scope by the preferred embodiments herein disclosed, since these embodiments are intended as illustrations of several aspects of the invention. Any equivalent embodiments are intended to be within the scope of this invention. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description. Such modifications are also intended to fall within the scope of the appended claims.

The entire disclosures of references cited herein are incorporated herein, in their entireties, for all purposes.

Citation or identification of a reference in this application or in connection with this application shall not be construed that such reference is available as prior art to the present invention.